PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

15 REFERENCES IN FILE CA (1907 TO DATE)
15 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> file hcaplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	180.35	180.56

FILE 'HCAPLUS' ENTERED AT 13:18:47 ON 19 MAR 2007
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

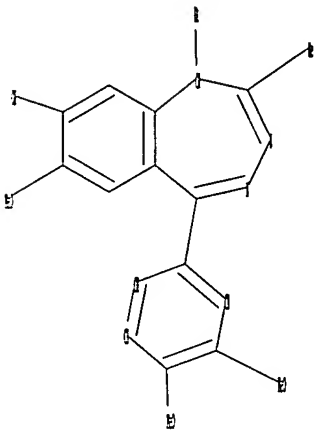
FILE COVERS 1907 - 19 Mar 2007 VOL 146 ISS 13
FILE LAST UPDATED: 18 Mar 2007 (20070318/ED)

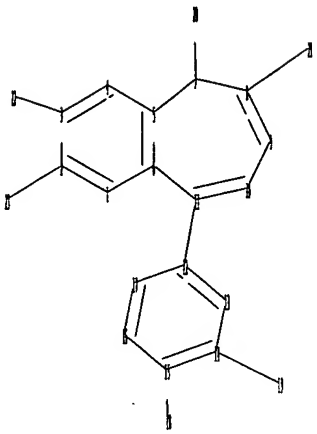
New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l3
L4 18 L3

Uploading C:\Program Files\Stnexp\Queries\10728261D.str





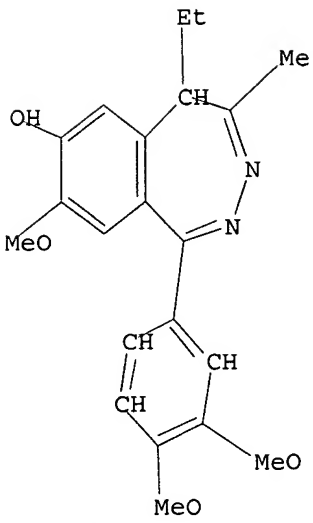
chain nodes :
18 19 20 21 22 23
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17
chain bonds :
2-23 3-22 7-20 8-21 11-12 14-19 15-18
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-11 7-8 8-9 9-10 10-11 12-13 12-17 13-14
14-15 15-16 16-17
exact/norm bonds :
3-22 5-7 6-11 7-8 8-9 9-10 10-11
exact bonds :
2-23 7-20 8-21 11-12 14-19 15-18
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6 12-13 12-17 13-14 14-15 15-16 16-17

G1:OH,MeO

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:CLASS 19:CLASS
20:CLASS 21:CLASS
22:CLASS 23:CLASS

L1 STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1 STR



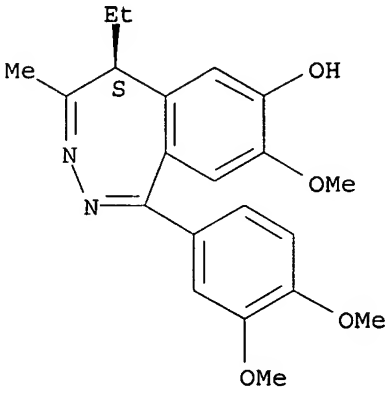
G1 OH,MeO

Structure attributes must be viewed using STN Express query preparation.

```
=> s l1
SAMPLE SEARCH INITIATED 13:17:57 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -       41 TO ITERATE

100.0% PROCESSED       41 ITERATIONS                                0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:          436 TO     1204
PROJECTED ANSWERS:               0 TO        0

L2             0 SEA SSS SAM L1

=> s l1 full
FULL SEARCH INITIATED 13:18:01 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -      642 TO ITERATE

100.0% PROCESSED      642 ITERATIONS                                4 ANSWERS
SEARCH TIME: 00.00.01

L3             4 SEA SSS FUL L1

=> d l3 1-
YOU HAVE REQUESTED DATA FROM 4 ANSWERS - CONTINUE? Y/(N):y

L3   ANSWER 1 OF 4  REGISTRY  COPYRIGHT 2007 ACS on STN
RN   792950-07-3  REGISTRY
ED   Entered STN:  06 Dec 2004
CN   5H-2,3-Benzodiazepin-7-ol, 1-(3,4-dimethoxyphenyl)-5-ethyl-8-methoxy-4-
     methyl-, (5S)-  (9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   (S)-1-(3,4-Dimethoxyphenyl)-4-methyl-5-ethyl-7-hydroxy-8-methoxy-5H-2,3-
     benzodiazepine
FS   STEREOSEARCH
MF   C21 H24 N2 O4
SR   CA
```

LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.

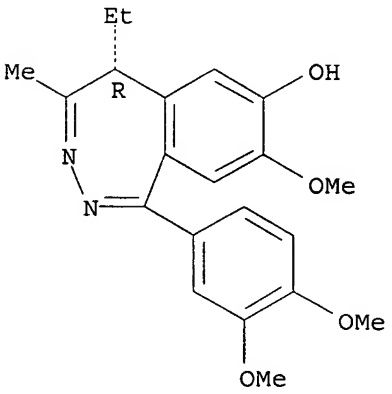


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

3 REFERENCES IN FILE CA (1907 TO DATE)
3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L3 ANSWER 2 OF 4 REGISTRY COPYRIGHT 2007 ACS on STN
RN 697754-50-0 REGISTRY
ED Entered STN: 23 Jun 2004
CN 5H-2,3-Benzodiazepin-7-ol, 1-(3,4-dimethoxyphenyl)-5-ethyl-8-methoxy-4-methyl-, (5R)- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN (R)-1-(3,4-Dimethoxyphenyl)-4-methyl-5-ethyl-7-hydroxy-8-methoxy-5H-2,3-benzodiazepine
FS STEREOSEARCH
MF C21 H24 N2 O4
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPAT2, USPATFULL

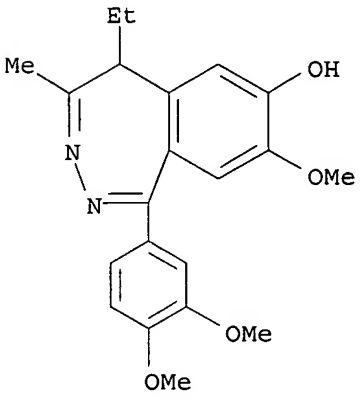
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

7 REFERENCES IN FILE CA (1907 TO DATE)
7 REFERENCES IN FILE CAPLUS (1907 TO DATE)

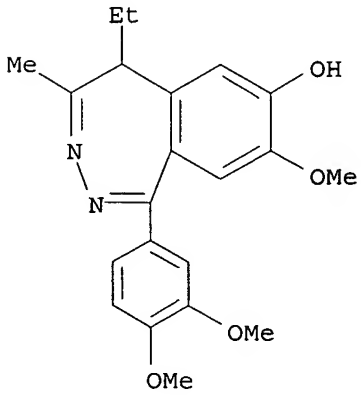
L3 ANSWER 3 OF 4 REGISTRY COPYRIGHT 2007 ACS on STN
RN 74950-20-2 REGISTRY
ED Entered STN: 16 Nov 1984
CN 5H-2,3-Benzodiazepin-7-ol, 1-(3,4-dimethoxyphenyl)-5-ethyl-8-methoxy-4-methyl-, monohydrochloride (9CI) (CA INDEX NAME)
MF C21 H24 N2 O4 . Cl H
LC STN Files: CA, CAPLUS, USPATFULL
CRN (74950-18-8)



● HCl

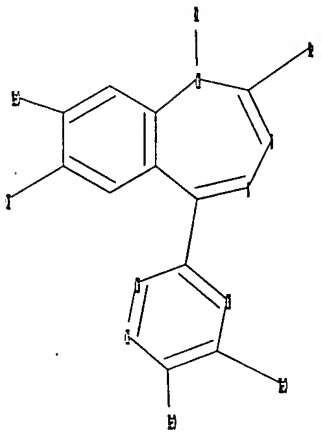
5 REFERENCES IN FILE CA (1907 TO DATE)
5 REFERENCES IN FILE CAPLUS (1907 TO DATE)

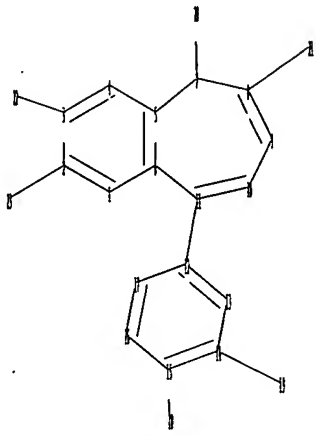
L3 ANSWER 4 OF 4 REGISTRY COPYRIGHT 2007 ACS on STN
RN 74950-18-8 REGISTRY
ED Entered STN: 16 Nov 1984
CN 5H-2,3-Benzodiazepin-7-ol, 1-(3,4-dimethoxyphenyl)-5-ethyl-8-methoxy-4-methyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 1-(3,4-Dimethoxyphenyl)-4-methyl-5-ethyl-7-hydroxy-8-methoxy-5H-2,3-benzodiazepine
MF C21 H24 N2 O4
CI COM
LC STN Files: CA, CAPLUS, TOXCENTER, USPAT2, USPATFULL



```
=> d hist

     (FILE 'HOME' ENTERED AT 13:17:02 ON 19 MAR 2007)

     FILE 'REGISTRY' ENTERED AT 13:17:39 ON 19 MAR 2007
L1                STRUCTURE UPLOADED
L2              0 S L1
L3              4 S L1 FULL

     FILE 'HCAPLUS' ENTERED AT 13:18:47 ON 19 MAR 2007
L4             18 S L3

     FILE 'REGISTRY' ENTERED AT 13:20:41 ON 19 MAR 2007
L5                STRUCTURE UPLOADED
L6              3 S L5 FULL

     FILE 'HCAPLUS' ENTERED AT 13:21:18 ON 19 MAR 2007
L7             12 S L6
L8             19 DUP REM L4 L7 (11 DUPLICATES REMOVED)
```

Uploading C:\Program Files\Stnexp\Queries\10728261E.str





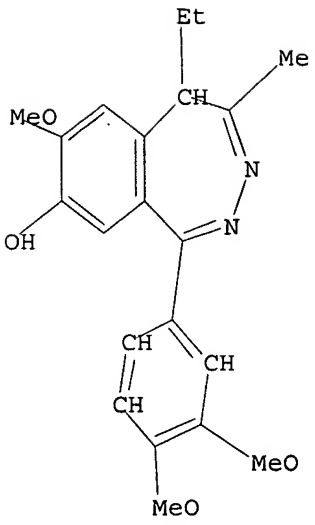
chain nodes :
18 19 20 21 22 23
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17
chain bonds :
2-23 3-22 7-20 8-21 11-12 14-19 15-18
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-11 7-8 8-9 9-10 10-11 12-13 12-17 13-14
14-15 15-16 16-17
exact/norm bonds :
2-23 5-7 6-11 7-8 8-9 9-10 10-11
exact bonds :
3-22 7-20 8-21 11-12 14-19 15-18
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6 12-13 12-17 13-14 14-15 15-16 16-17

G1:OH,MeO

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:CLASS 19:CLASS
20:CLASS 21:CLASS
22:CLASS 23:CLASS

L5 STRUCTURE UPLOADED

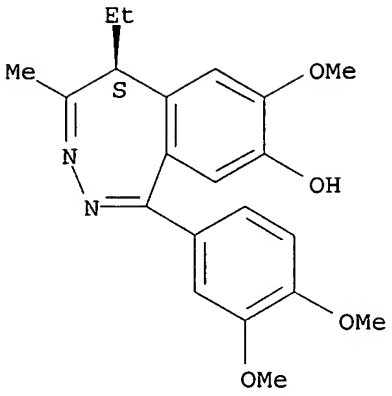
=> d l5
L5 HAS NO ANSWERS
L5 STR



G1 OH,MeO

Structure attributes must be viewed using STN Express query preparation.

```
=> s l5 full
FULL SEARCH INITIATED 13:21:03 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -      642 TO ITERATE

100.0% PROCESSED      642 ITERATIONS                                3 ANSWERS
SEARCH TIME: 00.00.01

L6             3 SEA SSS FUL L5

=> d l6 1-
YOU HAVE REQUESTED DATA FROM 3 ANSWERS - CONTINUE? Y/(N):y

L6   ANSWER 1 OF 3  REGISTRY  COPYRIGHT 2007 ACS on STN
RN   702693-86-5  REGISTRY
ED   Entered STN:  02 Jul 2004
CN   5H-2,3-Benzodiazepin-8-ol, 1-(3,4-dimethoxyphenyl)-5-ethyl-7-methoxy-4-
     methyl-, (5S)- (9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   (S)-1-(3,4-Dimethoxyphenyl)-4-methyl-5-ethyl-7-methoxy-8-hydroxy-5H-2,3-
     benzodiazepine
FS   STEREOSEARCH
MF   C21 H24 N2 O4
SR   CA
LC   STN Files:   CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.
```

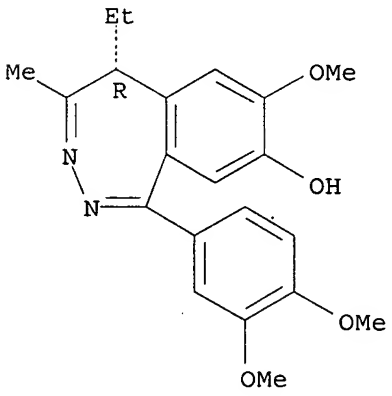


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

5 REFERENCES IN FILE CA (1907 TO DATE)
5 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L6 ANSWER 2 OF 3 REGISTRY COPYRIGHT 2007 ACS on STN
RN 697754-53-3 REGISTRY
ED Entered STN: 23 Jun 2004
CN 5H-2,3-Benzodiazepin-8-ol, 1-(3,4-dimethoxyphenyl)-5-ethyl-7-methoxy-4-methyl-, (5R)- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN (R)-1-(3,4-Dimethoxyphenyl)-4-methyl-5-ethyl-7-methoxy-8-hydroxy-5H-2,3-benzodiazepine
FS STEREOSEARCH
MF C21 H24 N2 O4
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPAT2, USPATFULL

Absolute stereochemistry.

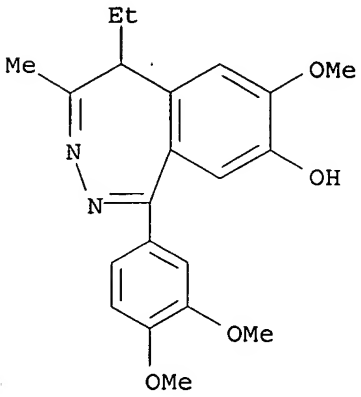


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

8 REFERENCES IN FILE CA (1907 TO DATE)
8 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L6 ANSWER 3 OF 3 REGISTRY COPYRIGHT 2007 ACS on STN
RN 95500-09-7 REGISTRY
ED Entered STN: 23 Mar 1985

CN 5H-2,3-Benzodiazepin-8-ol, 1-(3,4-dimethoxyphenyl)-5-ethyl-7-methoxy-4-methyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 1-(3,4-Dimethoxyphenyl)-4-methyl-5-ethyl-7-methoxy-8-hydroxy-5H-2,3-benzodiazepine
MF C21 H24 N2 O4
LC STN Files: CA, CAPLUS, TOXCENTER, USPAT2, USPATFULL



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

10 REFERENCES IN FILE CA (1907 TO DATE)
10 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> file hcaplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	177.95	461.17
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-14.04

FILE 'HCAPLUS' ENTERED AT 13:21:18 ON 19 MAR 2007
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 19 Mar 2007 VOL 146 ISS 13
FILE LAST UPDATED: 18 Mar 2007 (20070318/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

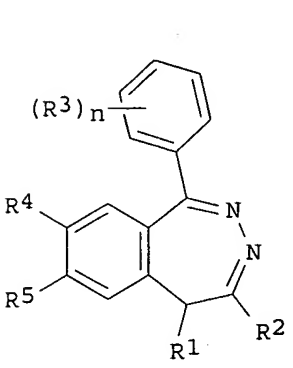
This file contains CAS Registry Numbers for easy and accurate

substance identification.

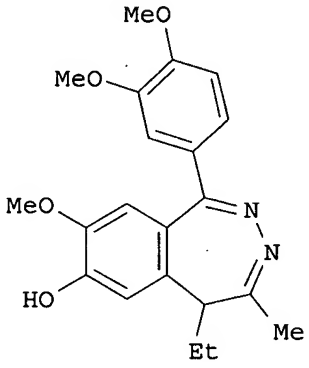
```
=> s l6
L7          12 L6
```

=> d ed abs ibib hitstr 1-
YOU HAVE REQUESTED DATA FROM 19 ANSWERS - CONTINUE? Y/(N):y

L8 ANSWER 1 OF 19 HCAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 1
ED Entered STN: 09 Feb 2007
GI



I



II

AB Compds. according to formula I, are administered at low dosage for the prevention or treatment of inflammatory disorders, particularly those affecting epithelial tissues such as those of the skin and gastrointestinal tract. Compds. of formula I wherein R1 is C1-7 hydrocarbyl, and C2-6 heteroalkyl; R2 is H and C1-7 hydrocarbyl; R1R2 may form a 5- to 6-membered carbocyclic or heterocyclic ring; R3 is OH and derivs., O-acyl, SH and derivs., NH2 and derivs., etc.; n is 1, 2, and 3; R4 is OH and derivs, SH and derivs., O-acyl, NH2, NH-acyl, and halo; R4R5 taken together to form 5- to 7-membered heterocyclic ring; and their pharmaceutically acceptable salts thereof, are claimed. Example compound II was prepared by cyclization of 1-(3-,4-dimethoxyphenyl)-3-methyl-4-ethyl-6,7-dimethoxyisobenzopyrilium chloride hydrochloride with hydrazine hydrate. All the invention compds. were evaluated for their LTB4 binding affinity.

ACCESSION NUMBER: 2007:151079 HCAPLUS <<LOGINID::20070319>>
DOCUMENT NUMBER: 146:229391
TITLE: Treatment of inflammatory disorders of the epithelium with low dose 2,3-benzodiazepines and their preparation
INVENTOR(S): Leventer, Steven M.; Kucharik, Robert F.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 37pp., Cont.-in-part of U.S. Ser. No. 727,940.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2007032479	A1	20070208	US 2006-578522	20060508
WO 2004050080	A1	20040617	WO 2003-US38643	20031203

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2004138209 A1 20040715 US 2003-727940 20031203

WO 2005056017 A1 20050623 WO 2004-US40403 20041203

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:

US 2003-727940	A2	20031203
WO 2003-US338643	A	20031203
WO 2004-US40403	W	20041203
US 2002-309573	A2	20021203
WO 2003-US38643	A	20031203

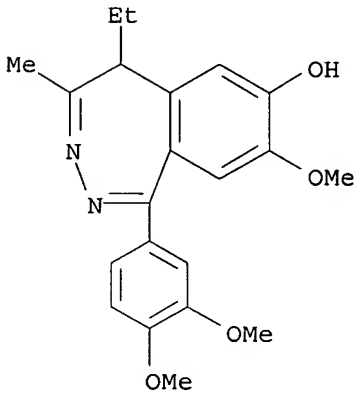
IT 74950-18-8P

RL: PAC (Pharmacological activity); PEP (Physical, engineering or chemical process); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)

(drug candidate; preparation of benzodiazepines useful in treatment and prevention of inflammatory disorders, affecting epithelium)

RN 74950-18-8 HCAPLUS

CN 5H-2,3-Benzodiazepin-7-ol, 1-(3,4-dimethoxyphenyl)-5-ethyl-8-methoxy-4-methyl- (9CI) (CA INDEX NAME)



IT 697754-50-0P

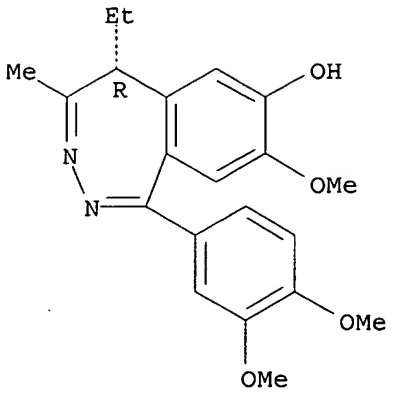
RL: PAC (Pharmacological activity); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(drug candidate; preparation of benzodiazepines useful in treatment and prevention of inflammatory disorders, affecting epithelium)

RN 697754-50-0 HCAPLUS

CN 5H-2,3-Benzodiazepin-7-ol, 1-(3,4-dimethoxyphenyl)-5-ethyl-8-methoxy-4-methyl-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L8 ANSWER 2 OF 19 HCAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 2
ED Entered STN: 25 Nov 2005
AB The invention discloses stereospecific derivs. of 2,3-benzodiazepines (Markush included) as inhibitors of phosphodiesterases, in particular phosphodiesterases 2 and 4, and their therapeutic use, particularly for the prevention and treatment of disease implying a central and/or peripheral disorder.

ACCESSION NUMBER: 2005:1242221 HCAPLUS <<LOGINID::20070319>>
DOCUMENT NUMBER: 144:643
TITLE: Benzodiazepine derivative phosphodiesterase inhibitors, and their therapeutic use
INVENTOR(S): Bernard, Philippe Pierre
PATENT ASSIGNEE(S): Greenpharma S.A., Fr.
SOURCE: Fr. Demande, 41 pp.
CODEN: FRXXBL
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 2870539	A1	20051125	FR 2004-5510	20040519
FR 2870539	B1	20060804		
WO 2005113517	A1	20051201	WO 2005-FR1260	20050519
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1761507	A1	20070314	EP 2005-773249	20050519
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR				

PRIORITY APPLN. INFO.: FR 2004-5510 A 20040519
WO 2005-FR1260 W 20050519

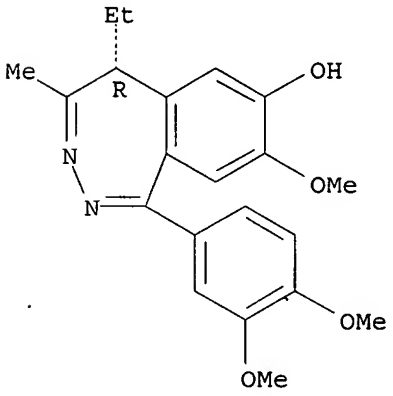
OTHER SOURCE(S): MARPAT 144:643
IT 697754-50-0 792950-07-3
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(benzodiazepine derivative phosphodiesterase inhibitors, and therapeutic use)

RN 697754-50-0 HCAPLUS

CN 5H-2,3-Benzodiazepin-7-ol, 1-(3,4-dimethoxyphenyl)-5-ethyl-8-methoxy-4-methyl-, (5R)- (9CI) (CA INDEX NAME)

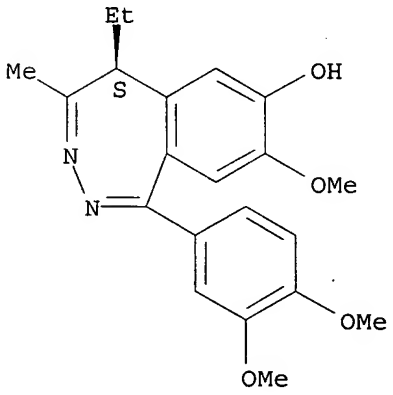
Absolute stereochemistry.



RN 792950-07-3 HCAPLUS

CN 5H-2,3-Benzodiazepin-7-ol, 1-(3,4-dimethoxyphenyl)-5-ethyl-8-methoxy-4-methyl-, (5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

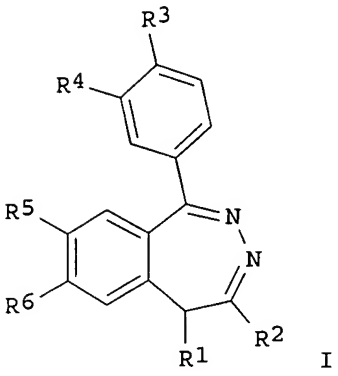


REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 3 OF 19 HCAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 3

ED Entered STN: 17 Dec 2004

GI



I

AB There is provided a method of modulating dopamine responses in the central nervous system of an individual or a method of treating a dopamine-mediated disorder in an individual not suffering from seizures or convulsions which comprises administering to the individual an effective amount of at least one compound of formula (I) [R1 = C1-7 hydrocarbyl or C2-6 heteroalkyl; R2 = H, C1-7 hydrocarbyl; wherein R1 and R2 may combine to form a carbocyclic or heterocyclic 5- or 6-membered ring; R3, R4, R5, R6 = OH, C1-7 hydrocarbyl, CF3, C1-7 hydrocarbyloxy, acyloxy, NH2, -NH(C1-6alkyl), -N(C1-6 alkyl)2, -NH-acyl, halogen; wherein R5 and R6 may combine to form a 5-, 6- or 7-membered heterocyclic ring] or pharmaceutically acceptable salts thereof or said compound comprising an (S)-enantiomer substantially free of the (R)-enantiomer of the same compound The above dopamine-mediated disorder comprises a neurol. disorder or a neuropsychiatric disorder. The neurol. disorder includes Huntington's chorea, Parkinson's disease, periodic limb movement syndrome, restless leg syndrome, hyperkinesias, Tourette's syndrome, Pick's disease, punch drunk syndrome, progressive subnuclear palsy, multiple systems atrophy, Landau-Kleffner syndrome, benign essential blepharospasm, amyotrophic lateral sclerosis, medication-induced movement disorders, and cognitive disorders. The neuropsychiatric disorder includes psychosis, personality disorders, psychiatric mood disorders, conduct and impulse disorders, schizophrenia, bipolar disorders, dysphoric mania, anxiety disorders, depression, panic disorders, agoraphobia, obsessive-compulsive disorders and eating disorders. Thus, 4.41 g (10 mmol) 1-(3,4-dimethoxyphenyl)-3-methyl-4-ethyl-6,7-dimethoxyisobenzopyrilium chloride hydrochloride was dissolved in methanol (35 mL) at a temperature of 40°. After cooling to 20-25°, hydrazine hydrate (0.75 g, 15 mmol, dissolved in 5 mL methanol) was added and the resulting mixture was allowed to react while monitoring the reaction by HPLC and when complete, was evaporated to dryness. The residue was triturated with cold water (3 mL), filtered and dried to yield the crude 1-(3,4-dimethoxyphenyl)-4-methyl-5-ethyl-7-hydroxy-8-methoxy-5H-2,3-benzodiazepine (racemic tofisopam) which was subsequently triturated with hot EtOAc to yield the pure product. Racemic tofisopam was resolved by a Chirobiotic V column (ASTEAC, Whippany, N.J.) to give (R)-tofisopam and (S)-tofisopam. (R)-tofisopam did not affect apomorphine-induced hypothermia in mice. Racemic tofisopam at 64 mg/kg tended to behave as a weak dopamine antagonist, i.e., lowering the rectal temperature at the thirty and sixty minute time points. However this trend was not statistically significant. (S)-tofisopam behaved as a weak dopamine antagonist at the 16 mg/kg dose at sixty minutes after apomorphine administration, i.e., showing a slight but statistically significant elevation in temperature At the higher doses, (S)-tofisopam demonstrated dopamine antagonism at both the thirty minute and sixty minute time points, i.e., lowering the rectal temperature at both time points.

ACCESSION NUMBER: 2004:1080692 HCAPLUS <<LOGINID::20070319>>
DOCUMENT NUMBER: 142:56375
TITLE: Modulation of dopamine responses with substituted

(S)-2,3-benzodiazepines

INVENTOR(S): Leventer, Steven M.; Harris, Herbert W.; Kucharik, Robert F.

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 33 pp.
CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004254173	A1	20041216	US 2003-461290	20030613

PRIORITY APPLN. INFO.: US 2003-461290 20030613

OTHER SOURCE(S): MARPAT 142:56375

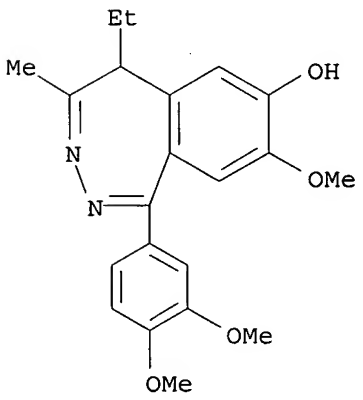
IT 74950-18-8P, 1-(3,4-Dimethoxyphenyl)-4-methyl-5-ethyl-7-hydroxy-8-methoxy-5H-2,3-benzodiazepine 792950-07-3P, (S)-1-(3,4-Dimethoxyphenyl)-4-methyl-5-ethyl-7-hydroxy-8-methoxy-5H-2,3-benzodiazepine

RL: PAC (Pharmacological activity); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of (S)-2,3-benzodiazepines for modulation of dopamine responses and treatment of neurol. disorders or neuropsychiatric disorders)

RN 74950-18-8 HCAPLUS

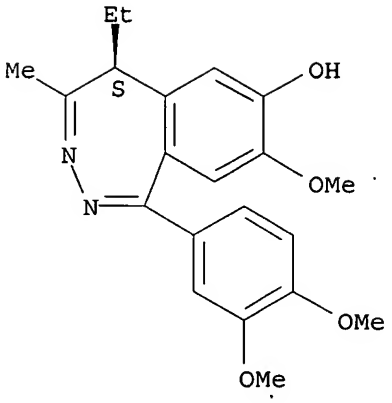
CN 5H-2,3-Benzodiazepin-7-ol, 1-(3,4-dimethoxyphenyl)-5-ethyl-8-methoxy-4-methyl- (9CI) (CA INDEX NAME)



RN 792950-07-3 HCAPLUS

CN 5H-2,3-Benzodiazepin-7-ol, 1-(3,4-dimethoxyphenyl)-5-ethyl-8-methoxy-4-methyl-, (5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L8 ANSWER 4 OF 19 HCAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 4
ED Entered STN: 19 Nov 2004
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to a preparation of 2,3-benzodiazepine derivs. of formula I [wherein: R1 is hydrocarbyl or heteroalkyl; R2 is H or hydrocarbyl; R1 and R2 may combine to form a (carbo/hetero)cyclic ring; R3 and R4 are independently selected from OH, SH, NO2, halogen, or S-alkyl, etc.; R5 is substituted phenyl], useful as antipyretic agents. For instance, (S)-2,3-benzodiazepine derivative II was prepared via heterocyclization of diketone III with hydrazine and subsequent resolution The prepared title compds. were tested in stress-induced hypothermia assay. (S)-enantiomer of tofisopam showed higher activity than the racemate or the (R)-enantiomer [dose: 64 mg/kg, (S)-tofisopam: 33 °C, (R)-tofisopam: 35.25 °C, racemate: 33.75 °C].

ACCESSION NUMBER: 2004:995773 HCAPLUS <<LOGINID::20070319>>
DOCUMENT NUMBER: 141:410971
TITLE: A preparation of 2,3-benzodiazepine derivatives, useful as antipyretic agents
INVENTOR(S): Harris, Herbert W.; Kucharik, Robert F.
PATENT ASSIGNEE(S): Vela Pharmaceuticals, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 23 pp., Cont.-in-part of U.S. Ser. No. 369,823.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

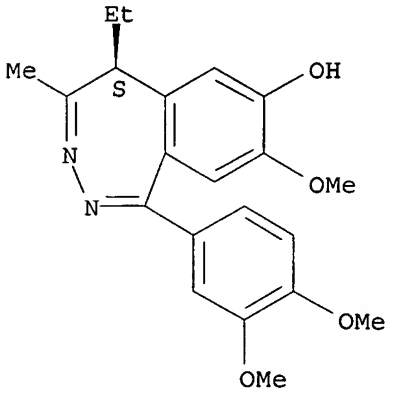
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004229866	A1	20041118	US 2004-781422	20040217
US 2004162284	A1	20040819	US 2003-369823	20030219
US 2004224943	A1	20041111	US 2004-827839	20040419

PRIORITY APPLN. INFO.: US 2003-369823 A2 20030219
US 2004-781422 A2 20040217
OTHER SOURCE(S): MARPAT 141:410971

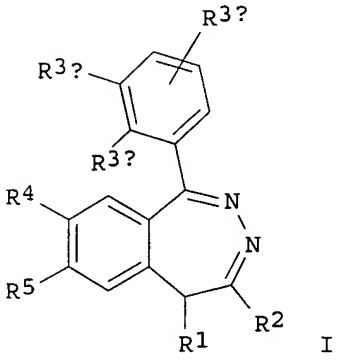
IT 792950-07-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of benzodiazepine derivs. useful as antipyretic agents)
RN 792950-07-3 HCAPLUS
CN 5H-2,3-Benzodiazepin-7-ol, 1-(3,4-dimethoxyphenyl)-5-ethyl-8-methoxy-4-methyl-, (5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L8 ANSWER 5 OF 19 HCAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 5
ED Entered STN: 12 Nov 2004
GI



I

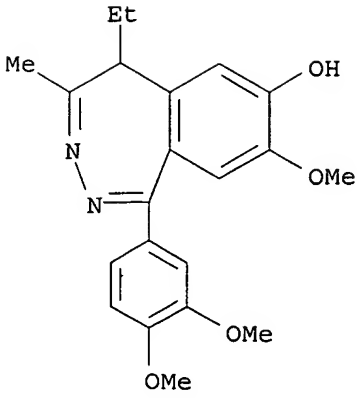
AB An (R)-2,3-benzodiazepine of formula (I) [R1 = C1-7 hydrocarbyl, C2-6 heteroalkyl; R2 = H, C1-7 hydrocarbyl; or R1 and R2 may combine to form a carbocyclic or heterocyclic 5- or 6-membered ring; R3a, R3b, R3c = H, -O-C1-7 hydrocarbyl, OH, -OC(O)-C1-6 alkyl, -OC(O)O-C1-7 hydrocarbyl, SH, -S-C1-3 alkyl, NH2, -NH-C1-6 alkyl, -N(C1-6 alkyl)2, -NH(:O)-C1-6 alkyl, NO2, halogen; provided at least one of R3a, R3b and R3c is other than H; R4, R5 = -O-C1-7 hydrocarbyl, OH, -OC(O)-C1-6 alkyl, -OC(O)O-C1-7 hydrocarbyl, SH, -S-C1-3 alkyl, NH2, -NH-C1-6 alkyl, -N(C1-6 alkyl)2, -NH(:O)-C1-6 alkyl, NO2, halo; or R4 and R5 may combine to form a 5-, 6- or 7-membered heterocyclic ring], substantially free from the corresponding (S)-enantiomer thereof with respect to the absolute conformation at the 5-position of the benzodiazepine ring, is administered to lower the body temperature of an individual. More specifically, the administered compound is (R)-tofisopam, or a pharmaceutically-acceptable salt thereof and said

individual is afflicted with a disorder associated with an elevated body temperature such as fever, malignant hyperthermia, serotonin syndrome, or hot flashes during menopause or perimenopause or occurred as side effects of drug therapy or subsequent to the removal of estrogen-producing tissue. Furthermore said individual is afflicted with a disorder such as cerebral ischemia or stroke wherein therapeutic benefit is achieved by lowering of the body temperature to a level below the normal body temperature Thus, 4.41 g (10 mmol) 1-(3,4-dimethoxyphenyl)-3-methyl-4-ethyl-6,7-dimethoxyisobenzopyrylium chloride hydrochloride was dissolved in methanol (35 mL) at 40°, cooled to 20-25°, treated with a solution of hydrazine hydrate (0.75 g, 15 mmol)in 5 mL methanol, and allowed to reaction. The reaction was monitored by HPLC and when complete, was evaporated to dryness. The residue is triturated with cold water (3 mL), filtered, and dried to yield crude (RS)-1-(3,4-dimethoxyphenyl)-4-methyl-5-ethyl-7-hydroxy-8-methoxy-5H-2,3-benzodiazepine (racemic tofisopam). Racemic tofisopam was resolved by chiral chromatog. using a semipreparative Chirobiotic V column (ASTEC, Whippany, New Jersey) and Me tert-Bu ether/MeCN as the eluent to give (R)-tofisopam and (S)-tofisopam. In a stress induced hyperthermia assay using mice, racemic tofisopam demonstrated activity in lowering the core body temperature (S)-tofisopam was more active than either the racemate or the (R)-enantiomer. However, the (R)-enantiomer showed greater tolerability compared with either the racemate or the (S)-enantiomer. For example, the mice treated with the (R)-enantiomer showed less sedation, abnormal gait, or ptosis, decreased muscle tone, decreased lacrimation, or decreased reactivity to touch compared with either (S)-enantiomer or the racemate.

ACCESSION NUMBER: 2004:964818 HCAPLUS <<LOGINID::20070319>>
DOCUMENT NUMBER: 141:410972
TITLE: Preparation of (R)-2,3-benzodiazepine derivatives and method of lowering body temperature with them
INVENTOR(S): Leventer, Steven M.; Kucharik, Robert F.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 22 pp., Cont.-in-part of U.S. Ser. No. 781,422.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

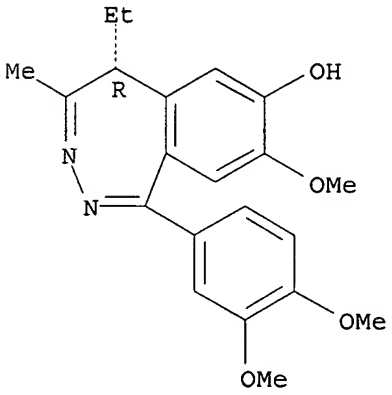
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004224943	A1	20041111	US 2004-827839	20040419
US 2004162284	A1	20040819	US 2003-369823	20030219
US 2004229866	A1	20041118	US 2004-781422	20040217
PRIORITY APPLN. INFO.:			US 2003-369823 A2	20030219
			US 2004-781422 A2	20040217

OTHER SOURCE(S): MARPAT 141:410972
IT 74950-18-8P, 1-(3,4-Dimethoxyphenyl)-4-methyl-5-ethyl-7-hydroxy-8-methoxy-5H-2,3-benzodiazepine 697754-50-0P, (R)-1-(3,4-Dimethoxyphenyl)-4-methyl-5-ethyl-7-hydroxy-8-methoxy-5H-2,3-benzodiazepine
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of (R)-2,3-benzodiazepine derivs. for lowering body temperature in fever, malignant hyperthermia, serotonin syndrome, or hot flashes)
RN 74950-18-8 HCAPLUS
CN 5H-2,3-Benzodiazepin-7-ol, 1-(3,4-dimethoxyphenyl)-5-ethyl-8-methoxy-4-methyl- (9CI) (CA INDEX NAME)



RN 697754-50-0 HCAPLUS
CN 5H-2,3-Benzodiazepin-7-ol, 1-(3,4-dimethoxyphenyl)-5-ethyl-8-methoxy-4-methyl-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L8 ANSWER 6 OF 19 HCAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 6
ED Entered STN: 16 Jul 2004
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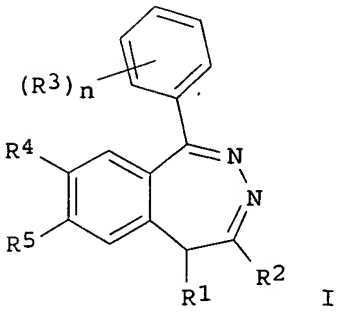


I

AB Claimed is a method of increasing the absolute neutrophil count in an

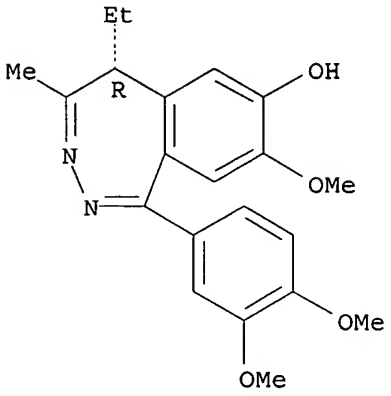
individual, comprising administering to said individual an effective amount of at least one compound according to formula (I) [R1 = C1-7 hydrocarbyl, C2-6 heteroalkyl; R2 = H, C1-7 hydrocarbyl; wherein R1 and R2 may combine to form a carbocyclic or heterocyclic 5- or 6-membered ring; R3 is independently selected from the group consisting of C1-6 alkoxy, OH, acyloxy, SH, C1-3 alkylthio, NH2, C1-6 alkylamino, di(C1-6 alkyl)amino, acylamino, NO2 and halogen; n = 1, 2 or 3; R4 and R5 are independently selected from the group consisting of C1-6 alkoxy, OH, acyloxy, SH, C1-3 alkylthio, NH2, acylamino, and halogen; wherein, R4 and R5 may combine to form a 5, 6 or 7-membered heterocyclic ring] or pharmaceutically-acceptable salts thereof. Also claimed is a method of treating an individual afflicted with neutropenia or preventing neutropenia in an individual who is at risk of developing neutropenia, comprising administering to said individual an effective amount of at least one compound I. The neutropenia treated is a side effect of exposure of an individual to ionizing radiation, in particular in therapeutic radiation therapy or the neutropenia developed is associated with immunodeficiency, in particular cancer or virus such as immunodeficiency virus. Thus, 4.41 g (10 mmol) 1-(3,4-dimethoxyphenyl)-3-methyl-4-ethyl-6,7-dimethoxyisobenzopyrilium chloride hydrochloride was dissolved in 35 mL MeOH at 40°, cooled to 20-25°, treated with a solution of hydrazine hydrate (0.75 g, 15 mmol) in 5 mL MeOH, allowed to react while monitoring by HPLC and when complete, evaporated to dryness, triturated with cold water (3 mL), filtered, dried to yield the crude 1-(3,4-dimethoxyphenyl)-4-methyl-5-ethyl-7-hydroxy-8-methoxy-5H-2,3-benzodiazepine which was subsequently triturated with hot EtOAc to give the pure product. (R)-1-(3,4-dimethoxyphenyl)-4-methyl-5-ethyl-7,8-dimethoxy-5H-2,3-benzo diazepine [(R)-tofisopam] significantly increased the neutrophil levels in a dose-dependently manner, e.g. by 29, 47, and 63% at 100, 200, 400 mg/kg/day, resp., for 15 days in female CD(SD)IGS BR rats.

ACCESSION NUMBER: 2004:569860 HCAPLUS <<LOGINID::20070319>>
DOCUMENT NUMBER: 141:123661
TITLE: Method of increasing neutrophil production using 2,3-benzodiazepines
INVENTOR(S): Harris, Herbert W.; Kucharik, Robert F.
PATENT ASSIGNEE(S): Vela Pharmaceuticals, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 29 pp., Cont.-in-part of U.S. Ser. No. 309,527.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

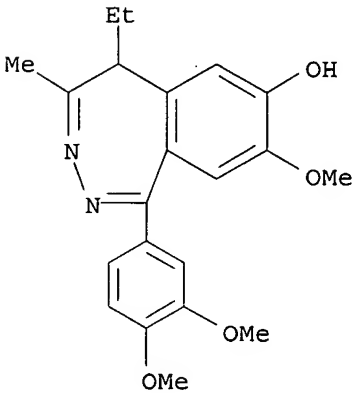
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004138210	A1	20040715	US 2003-728286	20031202
US 2004106601	A1	20040603	US 2002-309527	20021203
US 7022700	B2	20060404		

PRIORITY APPLN. INFO.: US 2002-309527 A2 20021203
OTHER SOURCE(S): MARPAT 141:123661
IT 697754-50-0P, (R)-1-(3,4-Dimethoxyphenyl)-4-methyl-5-ethyl-7-hydroxy-8-methoxy-5H-2,3-benzodiazepine
RL: PAC (Pharmacological activity); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of benzodiazepines for increasing neutrophil production to prevent or treat neutropenia developed as side effect of exposure to ionizing radiation in therapeutic radiation therapy.)
RN 697754-50-0 HCAPLUS
CN 5H-2,3-Benzodiazepin-7-ol, 1-(3,4-dimethoxyphenyl)-5-ethyl-8-methoxy-4-methyl-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 74950-18-8P, 1-(3,4-Dimethoxyphenyl)-4-methyl-5-ethyl-7-hydroxy-8-methoxy-5H-2,3-benzodiazepine
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of benzodiazepines for increasing neutrophil production to prevent
or treat neutropenia developed as side effect of exposure to ionizing radiation in therapeutic radiation therapy.)
RN 74950-18-8 HCAPLUS
CN 5H-2,3-Benzodiazepin-7-ol, 1-(3,4-dimethoxyphenyl)-5-ethyl-8-methoxy-4-methyl- (9CI) (CA INDEX NAME)



L8 ANSWER 7 OF 19 HCAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 7
ED Entered STN: 16 Jul 2004
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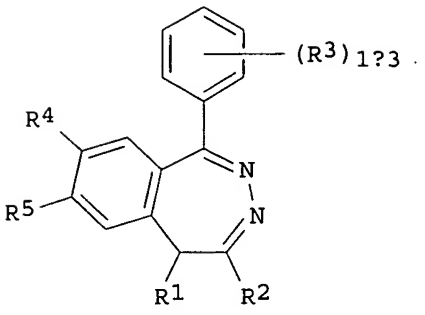

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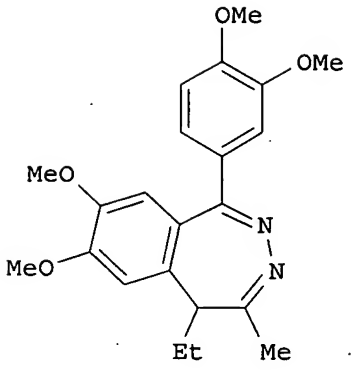


II

AB The invention relates to a preparation of 5H-2,3-benzodiazepine derivs. of formula I [wherein: R1 is (hetero)alkyl; R2 is H or alkyl; R3 is alkoxy, OH, SH, or NH2, etc.; R4 and R5 are independently selected from alkoxy, OH, NH2, NH-acyl, or halogens, etc.], useful for the treatment of inflammatory disorders, particularly inflammatory disorders mediated by LTB4. For instance, prepared (R)-5-ethyl-2,3-benzodiazepine derivative II was screened in LTB4 binding assay (Ki = 0.444 μM, table 2).

ACCESSION NUMBER: 2004:570503 HCAPLUS <<LOGINID::20070319>>
DOCUMENT NUMBER: 141:123662
TITLE: A preparation of 2,3-benzodiazepine derivatives, useful for the treatment of inflammatory disorders
INVENTOR(S): Kucharik, Robert F.; Harris, Herbert W.
PATENT ASSIGNEE(S): Vela Pharmaceuticals, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 32 pp., Cont.-in-part of U.S. Ser. No. 309,573.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004138209	A1	20040715	US 2003-727940	20031203
US 2004106602	A1	20040603	US 2002-309573	20021203
US 6864251	B2	20050308		
CA 2548038	A1	20050623	CA 2004-2548038	20041203
WO 2005056017	A1	20050623	WO 2004-US40403	20041203
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1689408	A1	20060816	EP 2004-812836	20041203
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS				
US 2007032479	A1	20070208	US 2006-578522	20060508

PRIORITY APPLN. INFO.:
US 2002-309573 A2 20021203
US 2003-727940 A 20031203
WO 2003-US338643 A 20031203
WO 2003-US38643 A 20031203

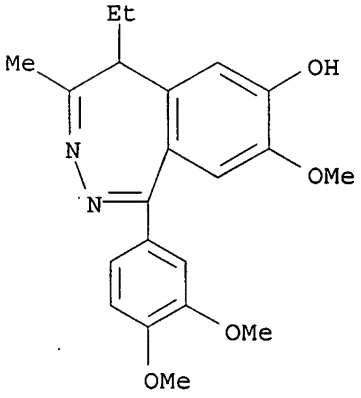
WO 2004-US40403 W 20041203

OTHER SOURCE(S): MARPAT 141:123662

IT 74950-18-8P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of benzodiazepine derivs. useful for the treatment of inflammatory disorders)

RN 74950-18-8 HCAPLUS

CN 5H-2,3-Benzodiazepin-7-ol, 1-(3,4-dimethoxyphenyl)-5-ethyl-8-methoxy-4-methyl- (9CI) (CA INDEX NAME)

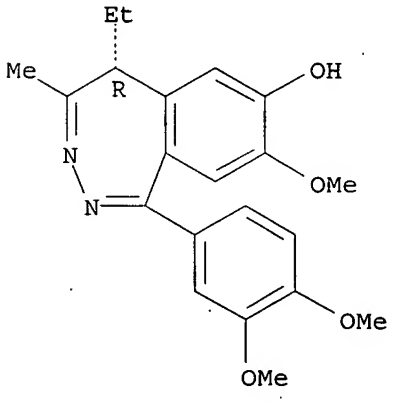


IT 697754-50-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of benzodiazepine derivs. useful for the treatment of inflammatory disorders)

RN 697754-50-0 HCAPLUS

CN 5H-2,3-Benzodiazepin-7-ol, 1-(3,4-dimethoxyphenyl)-5-ethyl-8-methoxy-4-methyl-, (5R)- (9CI) (CA INDEX NAME)

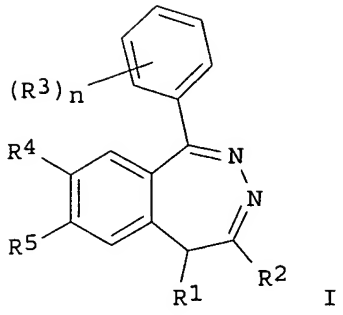
Absolute stereochemistry.



L8 ANSWER 8 OF 19 HCAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 8

ED Entered STN: 04 Jun 2004

GI



I

AB Disclosed is a method of treating an individual afflicted with an inflammatory disorder mediated by leukotriene B4 (LTB4) comprising administering to said individual an effective amount of at least one compound according to formula (I) [R1 = C1-7 hydrocarbyl, C2-6 heteroalkyl; R2 = H, C1-7 hydrocarbyl; or R1 and R2 may combine to form a carbocyclic or heterocyclic 5- or 6-membered ring; R3 = C1-6 alkoxy, OH, acyloxy, SH, C1-3 alkylthio, NH2, mono or di(C1-6 alkyl)amino, acylamino, NO2, halo; n = 1, 2, 3; R4, R5 = C1-6 alkoxy, OH, acyloxy, SH, C1-3 alkylthio, NH2, acylamino, halo; or R4 and R5 may combine to form a 5, 6 or 7-membered heterocyclic ring; wherein, the compds. according to this formula are (R)-enantiomers substantially free of the corresponding (S)-enantiomers, with respect to the absolute conformation at the 5-position of the benzodiazepine ring] or pharmaceutically acceptable salts thereof. Inflammatory disorders mediated by LTB4 include inflammatory bowel disease, ulcerative colitis, psoriasis, rheumatoid arthritis, Crohn's disease and radiation-induced gastrointestinal inflammation. Thus, 1-(3,4-dimethoxyphenyl)-3-methyl-4-ethyl-6,7-dimethoxyisobenzopyrilium chloride hydrochloride was cyclocondensed with hydrazine hydrate at 20-25° in MeOH gave (R,S)-1-(3,4-dimethoxyphenyl)-4-methyl-5-ethyl-7-hydroxy-8-methoxy-5H-2,3-benzodiazepine [(R,S)-II] which was resolved by a Chirobiotic V column (ASTEAC, whippany, N.J.) to give (R)-II. (R,S)-, (R)-, and (S)-1-(3,4-Dimethoxyphenyl)-4-methyl-5-ethyl-7,8-dimethoxy-5H-2,3-benzodiazepine (tofisopam) showed the binding affinity to LTB4 receptor with Ki of 4.52, 0.444, and 76.0 μM, resp.

ACCESSION NUMBER: 2004:451631 HCAPLUS <<LOGINID::20070319>>
DOCUMENT NUMBER: 141:23558
TITLE: Preparation of optically pure (R)-2,3-benzodiazepines for treatment of LTB4-mediated inflammatory disorders
INVENTOR(S): Kucharik, Robert F.; Harris, Herbert W.
PATENT ASSIGNEE(S): Vela Pharmaceuticals, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 27 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004106602	A1	20040603	US 2002-309573	20021203
US 6864251	B2	20050308		
CA 2508312	A1	20040617	CA 2003-2508312	20031203
WO 2004050080	A1	20040617	WO 2003-US38643	20031203

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,

LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN,
TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE,
ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK,
TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2003298913	A1	20040623	AU 2003-298913		20031203
US 2004138209	A1	20040715	US 2003-727940		20031203
EP 1581206	A1	20051005	EP 2003-796673		20031203
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
JP 2006510635	T	20060330	JP 2004-557607		20031203
PRIORITY APPLN. INFO.:			US 2002-309573	A	20021203
			WO 2003-US38643	W	20031203

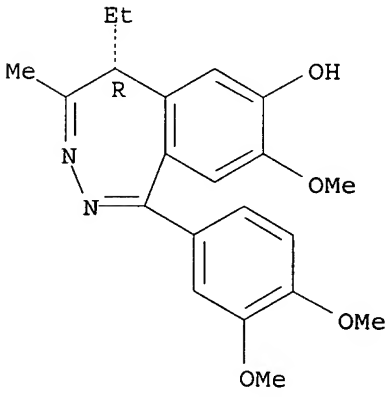
OTHER SOURCE(S): MARPAT 141:23558

IT 697754-50-0P, (R)-1-(3,4-Dimethoxyphenyl)-4-methyl-5-ethyl-7-hydroxy-8-methoxy-5H-2,3-benzodiazepine
RL: PAC (Pharmacological activity); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of optically pure (R)-2,3-benzodiazepines for treatment of LTB4-mediated inflammatory disorders)

RN 697754-50-0 HCAPLUS

CN 5H-2,3-Benzodiazepin-7-ol, 1-(3,4-dimethoxyphenyl)-5-ethyl-8-methoxy-4-methyl-, (5R)- (9CI) (CA INDEX NAME)

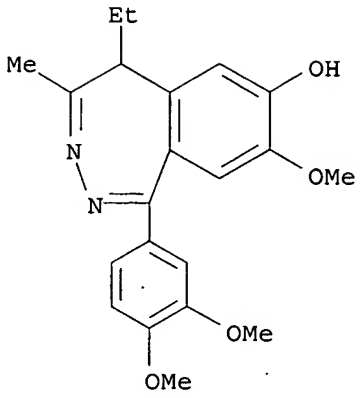
Absolute stereochemistry.



IT 74950-18-8P, 1-(3,4-Dimethoxyphenyl)-4-methyl-5-ethyl-7-hydroxy-8-methoxy-5H-2,3-benzodiazepine
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of optically pure (R)-2,3-benzodiazepines for treatment of LTB4-mediated inflammatory disorders)

RN 74950-18-8 HCAPLUS

CN 5H-2,3-Benzodiazepin-7-ol, 1-(3,4-dimethoxyphenyl)-5-ethyl-8-methoxy-4-methyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 9 OF 19 HCAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 9
ED Entered STN: 04 Jun 2004
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [R1 = alkylhydrocarbyl, heteroalkyl; R2 = H, hydrocarbyl, wherein R1 and R2 may combine to form a carbocyclic or heterocyclic 5- or 6-membered ring; X = (R3)n; R3 = O-alkyl, OH, O-acyl, etc.; n = 1-3; R4, R5 = O-alkyl, OH, O-acyl, etc., wherein R4 and R5 may combine to form a 5-, 6-, 7-membered heterocyclic ring] and their pharmaceutically acceptable salts were prepared For example, condensation-cyclization of diketone II, e.g., prepared from 3-methoxy-4-hydroxybenzoic acid in 7-steps, and hydrazine hydrate afforded racemic benzodiazepine III. In a 16-day study of neutrophil production in rats, one example of compound I, e.g., R-tofisopam, significantly increased neutrophil levels in a dose-dependant manner. Compds. I are claimed useful for increasing the production of neutrophils.

ACCESSION NUMBER: 2004:451630 HCAPLUS <<LOGINID::20070319>>
DOCUMENT NUMBER: 141:23557
TITLE: Preparation of (R)-2,3-benzodiazepines for the treatment of neutropenia.
INVENTOR(S): Harris, Herbert W.; Kucharik, Robert F.
PATENT ASSIGNEE(S): Vela Pharmaceuticals, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 20 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004106601	A1	20040603	US 2002-309527	20021203
US 7022700	B2	20060404		
US 2004138210	A1	20040715	US 2003-728286	20031202
WO 2004050615	A2	20040617	WO 2003-US38634	20031203
WO 2004050615	A3	20040805		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,

LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN,
TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE,
ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK,
TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2003302682 A1 20040623 AU 2003-302682 20031203
PRIORITY APPLN. INFO.: US 2002-309527 A2 20021203
WO 2003-US38634 W 20031203

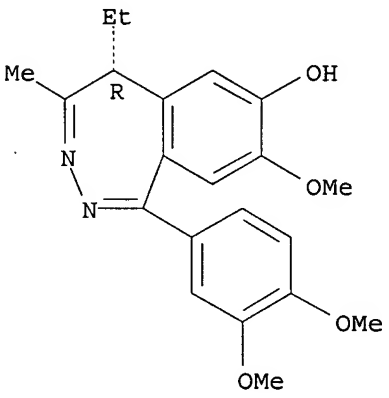
OTHER SOURCE(S): MARPAT 141:23557

IT 697754-50-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of benzodiazepines for the treatment of neutropenia.)

RN 697754-50-0 HCAPLUS

CN 5H-2,3-Benzodiazepin-7-ol, 1-(3,4-dimethoxyphenyl)-5-ethyl-8-methoxy-4-methyl-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L8 ANSWER 10 OF 19 HCAPLUS COPYRIGHT 2007 ACS on STN

ED Entered STN: 17 Jun 2004

AB Pharmaceutical compns. comprising 1-(3,4-dimethoxyphenyl)-4-methyl-5-ethyl-7-methoxy-8-hydroxy-5H-2,3-benzodiazepine (I) or a pharmaceutically acceptable salt thereof are described. The compns. are used for treating, preventing or delaying the onset of disorders mediated by LTB4, TXA2 or adenosine. For example, I demonstrated statistically significant anticonvulsant activity at 30 and 45 mg/kg doses. The 60 mg dose showed comparable anticonvulsant activity, but fell short of statistical significance. This is likely a consequence of the small number of tested animals,.

ACCESSION NUMBER: 2004:490707 HCAPLUS <<LOGINID::20070319>>

DOCUMENT NUMBER: 141:33842

TITLE: Pharmaceutical composition of 1-(3,4-dimethoxyphenyl)-4-methyl-5-ethyl-7-methoxy-8-hydroxy-5H-2,3-benzodiazepine and uses thereof

INVENTOR(S): Kucharik, Robert F.; Leventer, Steven M.; Harris, Herbrt W.

PATENT ASSIGNEE(S): Vela Pharmaceuticals, Inc., USA

SOURCE: PCT Int. Appl., 59 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004050040	A2	20040617	WO 2003-US38642	20031203
WO 2004050040	A3	20050331		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
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CA 2508542	A1	20040617	CA 2003-2508542	20031203
AU 2003293405	A1	20040623	AU 2003-293405	20031203
US 2004157833	A1	20040812	US 2003-728261	20031203
EP 1567161	A2	20050831	EP 2003-790352	20031203
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2006510634	T	20060330	JP 2004-557606	20031203

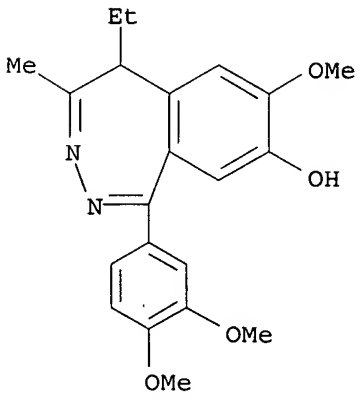
PRIORITY APPLN. INFO.:

US 2002-430771P	P	20021203
WO 2003-US38642	W	20031203

IT 95500-09-7P, 1-(3,4-Dimethoxyphenyl)-4-methyl-5-ethyl-7-methoxy-8-hydroxy-5H-2,3-benzodiazepine
RL: ANT (Analyte); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of benzodiazepine derivative for treatment of disorders mediated by
adenosine, LTB4 or TXA2)

RN 95500-09-7 HCAPLUS

CN 5H-2,3-Benzodiazepin-8-ol, 1-(3,4-dimethoxyphenyl)-5-ethyl-7-methoxy-4-methyl- (9CI) (CA INDEX NAME)

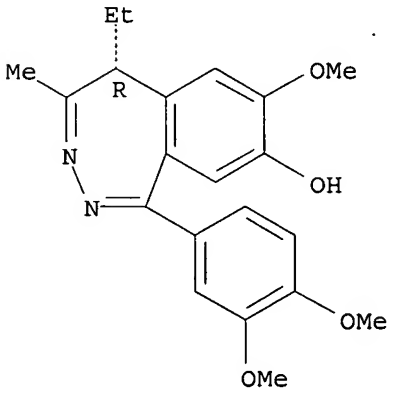


IT 697754-53-3P, (R)-1-(3,4-Dimethoxyphenyl)-4-methyl-5-ethyl-7-methoxy-8-hydroxy-5H-2,3-benzodiazepine 702693-86-5P
RL: PAC (Pharmacological activity); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of benzodiazepine derivative for treatment of disorders mediated by
adenosine, LTB4 or TXA2)

RN 697754-53-3 HCAPLUS

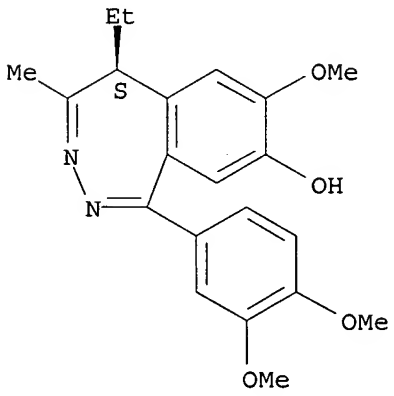
CN 5H-2,3-Benzodiazepin-8-ol, 1-(3,4-dimethoxyphenyl)-5-ethyl-7-methoxy-4-methyl-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

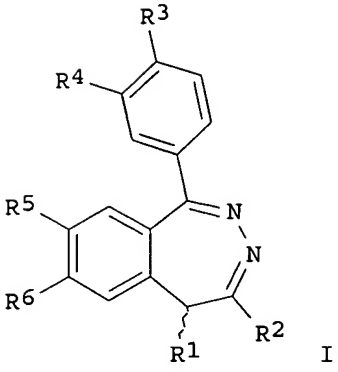


RN 702693-86-5 HCAPLUS
CN 5H-2,3-Benzodiazepin-8-ol, 1-(3,4-dimethoxyphenyl)-5-ethyl-7-methoxy-4-methyl-, (5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L8 ANSWER 11 OF 19 HCAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 10
ED Entered STN: 30 Oct 2003
GI



I

AB Title compds. [I; R1 = hydrocarbyl, heteroalkyl; R2 = H, hydrocarbyl; R1R2 = atoms to form a carbocyclic, heterocyclic 5-6 membered ring; 1 of R3-R6 = OH, and the rest = hydrocarbyl, CF3, hydrocarbyloxy, acyloxy, NH2, alkylamino, dialkylamino, acylamino, halo; R5R6 = atoms to form a 5-7 membered heterocyclic ring], were prepared Thus, 3-[2-[(3-hydroxy-4-methoxyphenyl)carbonyl]-4,5-dimethoxyphenyl]pentan-2-one (preparation given) and N2H4 were refluxed 0.5 h. in EtOH; the cooled solution was saturated with HCl gas, concentrated, basified with concentrated aqueous NH3, and extracted with CH2Cl2 to give 1-(3-hydroxy-4-methoxyphenyl)-4-methyl-5-ethyl-7,8-dimethoxy-5H-2,3-benzodiazepine. The latter at 32 mg/kg i.p. gave 42% inhibition in the glass bead test of colonic propulsive motility in mice.

ACCESSION NUMBER: 2003:851280 HCAPLUS <<LOGINID::20070319>>
DOCUMENT NUMBER: 139:350760
TITLE: Preparation of 2,3-benzodiazepines for treatment of irritable bowel syndrome and nonulcer dyspepsia.
INVENTOR(S): Harris, Herbert W.; Kucharik, Robert F.
PATENT ASSIGNEE(S): Vela Pharmaceuticals, Inc., USA
SOURCE: U.S., 18 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6638928	B1	20031028	US 2002-309526	20021203
CA 2508546	A1	20040617	CA 2003-2508546	20031203
WO 2004050616	A2	20040617	WO 2003-US38637	20031203
WO 2004050616	A3	20040910		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003297663	A1	20040623	AU 2003-297663	20031203
EP 1567162	A2	20050831	EP 2003-812516	20031203
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2006510632	T	20060330	JP 2004-557604	20031203

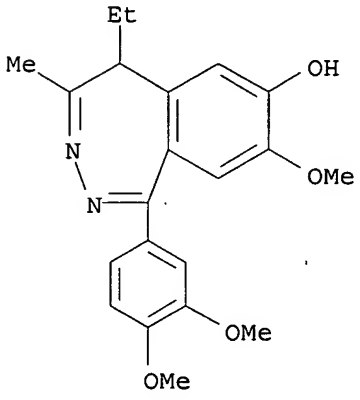
PRIORITY APPLN. INFO.: US 2002-309526 A 20021203
WO 2003-US38637 W 20031203

OTHER SOURCE(S): MARPAT 139:350760

IT 74950-18-8, 1-(3,4-Dimethoxyphenyl)-4-methyl-5-ethyl-7-hydroxy-8-methoxy-5H-2,3-benzodiazepine
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of benzodiazepines for treatment of irritable bowel syndrome and nonulcer dyspepsia)

RN 74950-18-8 HCAPLUS

CN 5H-2,3-Benzodiazepin-7-ol, 1-(3,4-dimethoxyphenyl)-5-ethyl-8-methoxy-4-methyl- (9CI) (CA INDEX NAME)

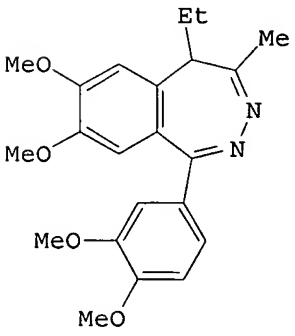


REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 12 OF 19 HCAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 11

ED Entered STN: 20 Apr 1985

GI

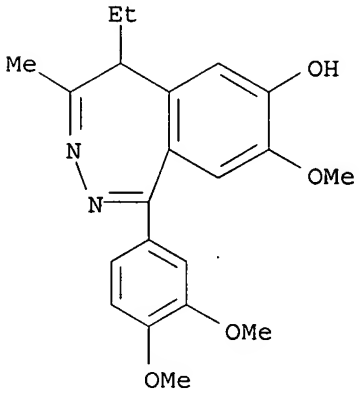


I

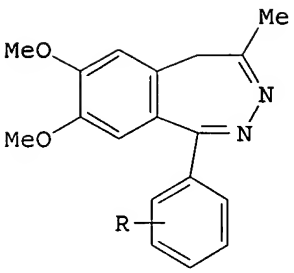
AB The biotransformation of tofizopam (I) [22345-47-7] was investigated after oral administration in animals and man. Most of the urinary metabolites were conjugated with glucuronic acid. The chief way of the metabolic information of tofizopam is demethylation, however, the demethylation site as well as the rate of the reaction was different in various species.

ACCESSION NUMBER: 1985:125037 HCAPLUS <<LOGINID::20070319>>

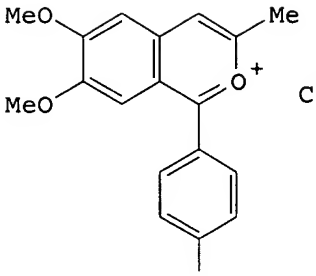
DOCUMENT NUMBER: 102:125037
TITLE: Investigation of metabolites of tofizopam in man and animals
AUTHOR(S): Tomori, Eva; Elekes, Istvan; Lang, Tibor; Horvath, Gyula
CORPORATE SOURCE: Inst. Drug Res., Budapest, H-1325, Hung.
SOURCE: Polish Journal of Pharmacology and Pharmacy (1984), 36(4), 423-30
CODEN: PJPPAA; ISSN: 0301-0244
DOCUMENT TYPE: Journal
LANGUAGE: English
IT 74950-18-8
RL: FORM (Formation, nonpreparative)
(formation of, as tofizopam metabolite in humans and laboratory animals)
RN 74950-18-8 HCAPLUS
CN 5H-2,3-Benzodiazepin-7-ol, 1-(3,4-dimethoxyphenyl)-5-ethyl-8-methoxy-4-methyl- (9CI) (CA INDEX NAME)



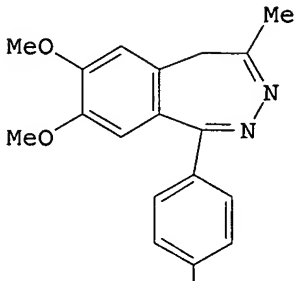
L8 ANSWER 13 OF 19 HCAPLUS COPYRIGHT 2007 ACS on STN
ED Entered STN: 12 May 1984
GI



I



II



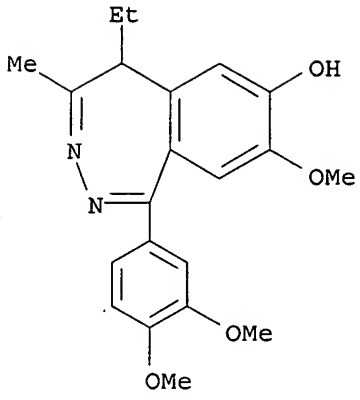
III

AB Benzodiazepines I (R = halogen, CF3) were prepared Thus, treatment of pyrylium salt II with N2H4 gave 72.5% III. I (R = 3-Cl) had a tranquilizer activity ED50 in the mouse fighting test of 16 mg/kg orally.

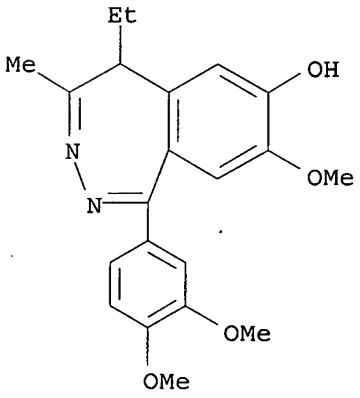
ACCESSION NUMBER: 1982:423830 HCAPLUS <<LOGINID::20070319>>
DOCUMENT NUMBER: 97:23830
TITLE: 5H-2,3-Benzodiazepine derivatives
INVENTOR(S): Korosi, Jeno; Lang, Tibor; Szekely, Jozsef; Andrasi, Ferenc; Zolyomi, Gabor; Borsi, Jozsef; Goldschmidt, Katali; Hamori, Tamas; Szabo, Gabriella; et al.
PATENT ASSIGNEE(S): Hung.
SOURCE: U.S., 7 pp. Cont.-in-part of U.S. Ser. No. 86,047, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4322346	A	19820330	US 1980-191811	19800926
HU 21372	A2	19811128	HU 1978-GO1426	19781019
HU 179018	B	19820828		

PRIORITY APPLN. INFO.: HU 1978-GO1426 A 19781019
US 1979-86047 A2 19791018
OTHER SOURCE(S): MARPAT 97:23830
IT 74950-18-8P 74950-20-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 74950-18-8 HCAPLUS
CN 5H-2,3-Benzodiazepin-7-ol, 1-(3,4-dimethoxyphenyl)-5-ethyl-8-methoxy-4-methyl- (9CI) (CA INDEX NAME)



RN 74950-20-2 HCAPLUS
CN 5H-2,3-Benzodiazepin-7-ol, 1-(3,4-dimethoxyphenyl)-5-ethyl-8-methoxy-4-methyl-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

L8 ANSWER 14 OF 19 HCAPLUS COPYRIGHT 2007 ACS on STN
ED Entered STN: 12 May 1984
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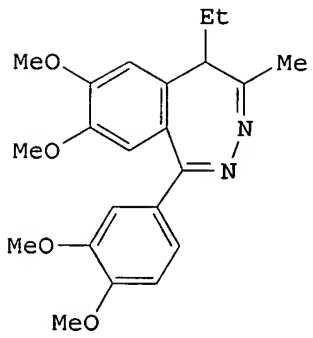
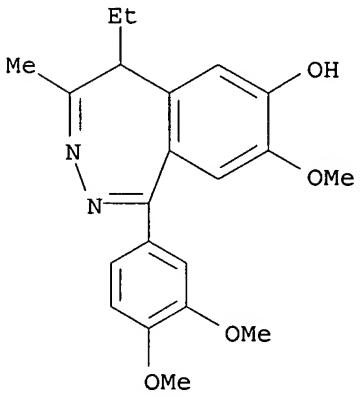


I

AB The metabolism of tofisopam (I) [22345-47-7] was studied in rats. Plasma pharmacokinetics and fecal excretion of I and its 5 demethyl metabolites were determined

ACCESSION NUMBER: 1981:508341 HCAPLUS <<LOGINID::20070319>>
DOCUMENT NUMBER: 95:108341
TITLE: Metabolic fate of tofisopam. 2. Metabolism of tofisopam in rats
AUTHOR(S): Kosuzume, Hiroshi; Ishiguro, Junzo; Kitamura, Yutaka; Ohnishi, Haruo; Kitagawa, Haruo
CORPORATE SOURCE: Res. Lab. Pharmacol., Mochida Pharm. Co. Ltd., Tokyo, Japan
SOURCE: Iyakuhin Kenkyu (1981), 12(2), 610-19
CODEN: IYKEDH; ISSN: 0287-0894
DOCUMENT TYPE: Journal
LANGUAGE: Japanese
IT 74950-18-8
RL: BIOL (Biological study)
(as tofisopam metabolite)
RN 74950-18-8 HCAPLUS
CN 5H-2,3-Benzodiazepin-7-ol, 1-(3,4-dimethoxyphenyl)-5-ethyl-8-methoxy-4-methyl- (9CI) (CA INDEX NAME)



L8 ANSWER 15 OF 19 HCAPLUS COPYRIGHT 2007 ACS on STN
ED Entered STN: 12 May 1984
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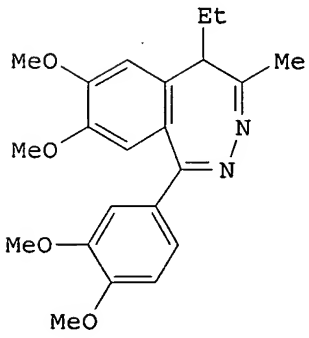


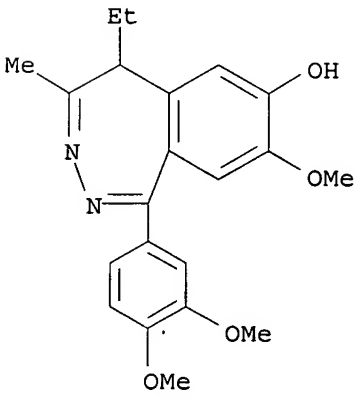
I

AB tofisopam (TF)(I) [22345-47-7] was similar to diazepam in its taming effects on rats and mice and in the inhibition of conflict in rats. However, its other effects such as potentiation of sleeping, reduction in motor coordination and muscle relaxation were much weaker than those of 1,4-benzodiazepines, and, therefore, these effects and the taming effects of TF were thought to be pharmacol. separable. TF did not show any affinity for the benzodiazepine receptor. TF had antiadrenaline, antinoradrenaline, and slight neuroleptic activities. It suppressed muricidal activity. Substituting an OH group for the methoxy group at the 7 and 8-positions of the 2,3-benzodiazepine ring and 3 and 4-position of the benzene ring of TF decreased its acute toxicity and all psychotropic activities. Antinoradrenaline activities of these related compds. were equivalent or less than those of TF. Apparently, the methoxy group in the chemical structure of TF is intrinsically related to its pharmacol. activities.

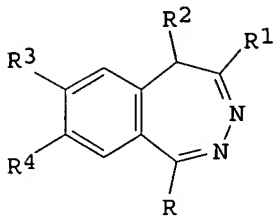
ACCESSION NUMBER: 1982:45875 HCAPLUS <<LOGINID::20070319>>
DOCUMENT NUMBER: 96:45875
TITLE: Behavioral pharmacological study on the structure activity relationship of benzodiazepine derivatives. With particular reference to activity of 2,3-benzodiazepine
AUTHOR(S): Ito, Chihiro
CORPORATE SOURCE: Dep. Pharmacol., Tokyo Med. Coll., Tokyo, Japan
SOURCE: Tokyo Ika Daigaku Zasshi (1981), 39(3), 369-84
CODEN: TIDZAH; ISSN: 0040-8905
DOCUMENT TYPE: Journal
LANGUAGE: Japanese

IT 74950-18-8
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(behavior and central nervous system response to, structure in relation to)

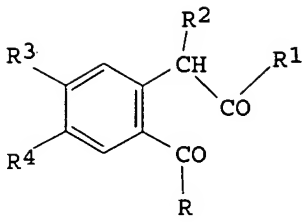
RN 74950-18-8 HCAPLUS
CN 5H-2,3-Benzodiazepin-7-ol, 1-(3,4-dimethoxyphenyl)-5-ethyl-8-methoxy-4-methyl- (9CI) (CA INDEX NAME)



L8 ANSWER 16 OF 19 HCAPLUS
ED Entered STN: 12 May 1984
GI



I



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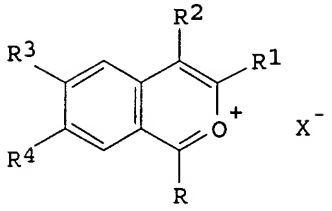
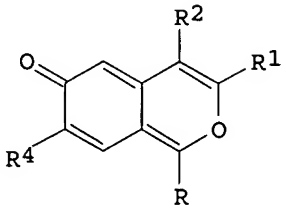
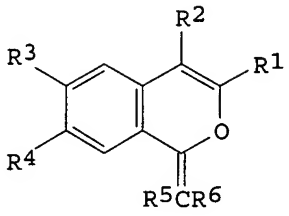


III



IV



V

AB 5H-2,3-Benzodiazepines I [R = H, alkyl, (substituted) amino, halo, OH, acyloxy, NO2, etc.; R1 = H, alkyl, CHO, CO2N, aryl, aralkoxy; R2 = H, alkyl, (substituted) amino, aryl; R3, R4 = H, halo, NO2, OH, NH2, alkoxy, aryl, etc.] were prepared by cyclization of N2H4 with II, III, IV, or V [X = anion, R5, R6 = H, alkyl, halo, OH, (substituted) amino, acyloxy, NO2, etc.]. I are enhancers of anesthetics. Thus, heating III (R = 4-ClC6H4, R1 = Me, R2 = H, R3 = R4 = MeO, X = ClO4) with N2H4 in MeOH to boil gave 72.5% corresponding I.

ACCESSION NUMBER: 1981:65733 HCAPLUS <<LOGINID::20070319>>
DOCUMENT NUMBER: 94:65733
TITLE: Benzodiazepines
PATENT ASSIGNEE(S): E. Gy. T. Gyogyszervegyeszeti Gyar, Hung.
SOURCE: Jpn. Kokai Tokkyo Koho, 15 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 55092377	A	19800712	JP 1979-134718	19791018
JP 63050354	B	19881007		
HU 21372	A2	19811128	HU 1978-GO1426	19781019
HU 179018	B	19820828		
AT 7906472	A	19830615	AT 1979-6472	19791004
AT 373589	B	19840210		
SE 7908481	A	19800420	SE 1979-8481	19791012
SE 439919	B	19850708		
SE 439919	C	19851017		
BE 879404	A1	19800415	BE 1979-9569	19791015
FI 7903209	A	19800420	FI 1979-3209	19791016
FI 66604	B	19840731		
FI 66604	C	19841112		
FR 2439189	A1	19800516	FR 1979-25698	19791016

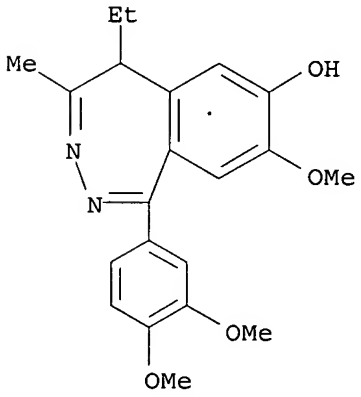
FR 2439189	B1	19841130			
AU 532079	B2	19830915	AU 1979-51817		19791016
CH 643835	A5	19840629	CH 1979-9292		19791016
CS 236456	B2	19850515	CS 1979-7020		19791016
DD 146596	A5	19810218	DD 1979-216290		19791017
DK 7904401	A	19800420	DK 1979-4401		19791018
DK 155327	B	19890328			
DK 155327	C	19890821			
NL 7907692	A	19800422	NL 1979-7692		19791018
NL 190552	B	19931116			
NL 190552	C	19940418			
NO 7903349	A	19800422	NO 1979-3349		19791018
NO 152048	B	19850415			
NO 152048	C	19850724			
ES 485163	A1	19800616	ES 1979-485163		19791018
CA 1125749	A1	19820615	CA 1979-337955		19791018
PL 124063	B1	19821231	PL 1979-219034		19791018
SU 1402258	A3	19880607	SU 1979-2832177		19791018

PRIORITY APPLN. INFO.: HU 1978-GO1426 A 19781019

IT 74950-18-8P 74950-20-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

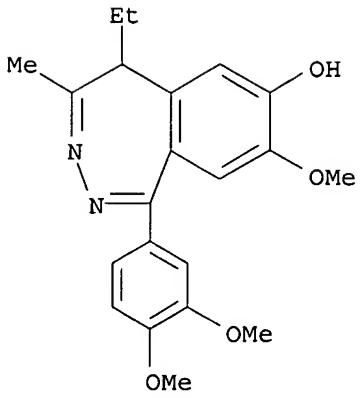
RN 74950-18-8 HCAPLUS

CN 5H-2,3-Benzodiazepin-7-ol, 1-(3,4-dimethoxyphenyl)-5-ethyl-8-methoxy-4-methyl- (9CI) (CA INDEX NAME)



RN 74950-20-2 HCAPLUS

CN 5H-2,3-Benzodiazepin-7-ol, 1-(3,4-dimethoxyphenyl)-5-ethyl-8-methoxy-4-methyl-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

L8 ANSWER 17 OF 19 HCAPLUS COPYRIGHT 2007 ACS on STN
ED Entered STN: 12 May 1984
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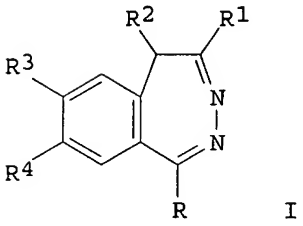


I

AB Benzodiazepines I (R = H, C1-5 alkyl, dialkylaminoalkyl, NH2, alkylamino, dialkylamino, styryl, optionally substituted aralkyl or aryl, heterocyclyl containing 1-2 N, O, and/or S atoms; R1 = H, C1-4 alkyl, CH2OH, CHO, CO2H, alkoxycarbonyl, heterocyclyl; R2 = H, C1-4 alkyl, dialkylaminoalkyl, alkylamino, dialkylamino, aryl; R3, R4 = H, halo, NO2, NH2, acyloxy, C1-3 alkyl, C1-5 alkoxy, dialkylaminoalkoxy, araloxy or R3R4 = methylenedioxy or carbonic acid residue) were prepared I have significant effects on the central nervous system, decreasing spontaneous motor activity and potentiating the effect of narcotics (assessed in mice). E.g., I (R = C6H4Cl-4, R1 = Me, R2 = H, R3 = R4 = OMe) was prepared by cyclocondensation of 1-(4-chlorophenyl)-3-methyl-6,7-dimethoxy-2-benzopyrylium perchlorate with N2H4.H20 (MeOH, reflux).

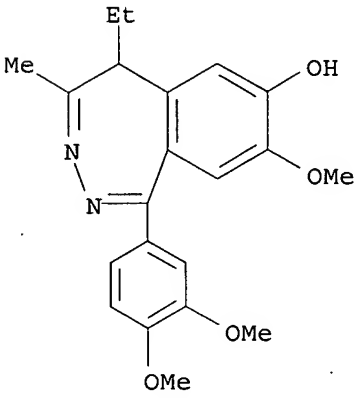
ACCESSION NUMBER: 1981:103443 HCAPLUS <<LOGINID::20070319>>
DOCUMENT NUMBER: 94:103443
TITLE: Benzodiazepines
INVENTOR(S): Korosi, Jeno; Lang, Tibor; Szekely, Jozsef; Anrasi, Ferenc; Zolyomi, Gabor; Borsy, Jozsef; Goldschmidt, Katalin; Hamori, Tames; Szabo, Gabriella; et al.
PATENT ASSIGNEE(S): E. Gy. T. Gyogyszervegyeszeti Gyar, Hung.
SOURCE: Brit. UK Pat. Appl., 14 pp.
CODEN: BAXXDU
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 2034706	A	19800611	GB 1979-36185	19791018
GB 2034706	B	19820804		

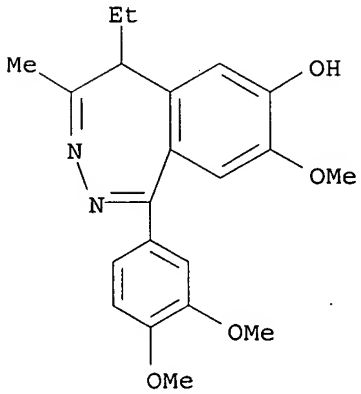
PRIORITY APPLN. INFO.: HU 1978-G1426 A 19781019

IT 74950-18-8P 74950-20-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as motor activity suppressant and narcotic potentiator)

RN 74950-18-8 HCAPLUS
CN 5H-2,3-Benzodiazepin-7-ol, 1-(3,4-dimethoxyphenyl)-5-ethyl-8-methoxy-4-methyl- (9CI) (CA INDEX NAME)

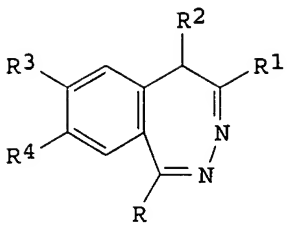


RN 74950-20-2 HCAPLUS
CN 5H-2,3-Benzodiazepin-7-ol, 1-(3,4-dimethoxyphenyl)-5-ethyl-8-methoxy-4-methyl-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

L8 ANSWER 18 OF 19 HCAPLUS COPYRIGHT 2007 ACS on STN
ED Entered STN: 12 May 1984
GI



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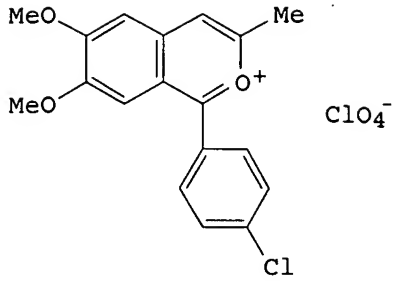

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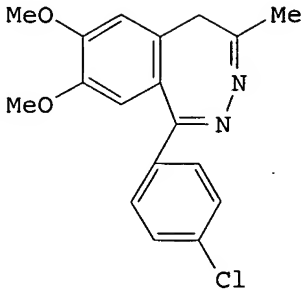


III

AB Benzodiazepines I [R = H, C1-5 alkyl, alkylamino, dialkylaminoalkyl, dialkylamino (optionally substituted), styryl, C7-10 phenylalkyl, O-, N-, or S-heterocyclyl; R1 = H, C1-4 alkyl, CH2OH, CHO, CO2H, carbalkoxy, optionally substituted acyl or aryl; R2 = H, optionally substituted acyl, aralkoxy, C1-4 alkyl, dialkylaminoalkyl or (di)alkylamino; R3R4 = OCH2O, carbonic acid moiety; R3, R4 independently = H, halo, NO2, NH2, OH, acyloxy, C1-3 alkyl optionally substituted with dialkylamino, carbalkoxy, C1-5 alkoxy, dialkylaminoalkyl, halo (un)substituted aralkoxy], useful as central nervous system depressants and narcotics potentiators (data tabulated), were prepared by several methods. Thus, treating NH2NH2.H2O with benzopyrylium salt II suspended in boiling MeOH gave 70.8% recrystd. benzodiazepine III. I (R = Ph, R1 = Me, R2 = Et, R3 = R4 = MeO) had ED50 35 mg/kg (mice) in inhibiting aggressiveness and gave 181% increase at 25 mg/kg (mice) in potentiation of hexobarbital Na.

ACCESSION NUMBER: 1980:568318 HCAPLUS <<LOGINID::20070319>>
DOCUMENT NUMBER: 93:168318

TITLE: 5H-2,3-Benzodiazepine derivatives and their pharmaceutical use

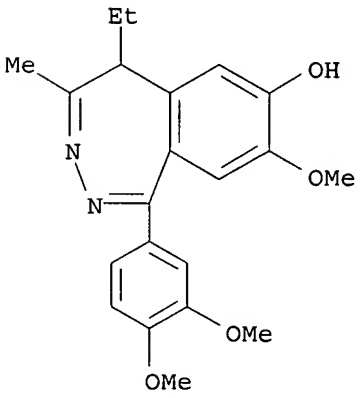
INVENTOR(S): Korosi, Jeno; Lang, Tibor; Szekely, Jozsef; Andrasi, Ferenc; Zolyomi, Gabor; Borsy, Jozsef; Goldschmidt, Katalin; Hamori, Tamas; Szabo, Gabriella; et al.
PATENT ASSIGNEE(S): E. Gy. T. Gyogyszervegyeszeti Gyar, Hung.

SOURCE: Ger. Offen., 78 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

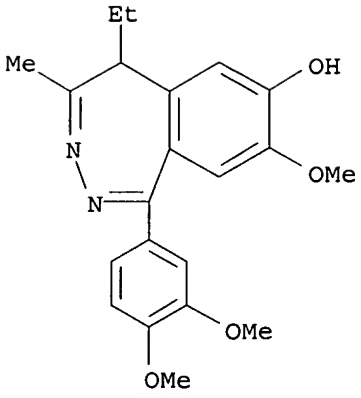
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 2940483	A1	19800430	DE 1979-2940483	19791005
DE 2940483	C2	19890622		
HU 21372	A2	19811128	HU 1978-GO1426	19781019
HU 179018	B	19820828		
AT 7906472	A	19830615	AT 1979-6472	19791004
AT 373589	B	19840210		
SE 7908481	A	19800420	SE 1979-8481	19791012
SE 439919	B	19850708		

SE 439919	C	19851017			
BE 879404	A1	19800415	BE 1979-9569		19791015
FI 7903209	A	19800420	FI 1979-3209		19791016
FI 66604	B	19840731			
FI 66604	C	19841112			
FR 2439189	A1	19800516	FR 1979-25698		19791016
FR 2439189	B1	19841130			
AU 532079	B2	19830915	AU 1979-51817		19791016
CH 643835	A5	19840629	CH 1979-9292		19791016
CS 236456	B2	19850515	CS 1979-7020		19791016
DD 146596	A5	19810218	DD 1979-216290		19791017
DK 7904401	A	19800420	DK 1979-4401		19791018
DK 155327	B	19890328			
DK 155327	C	19890821			
NL 7907692	A	19800422	NL 1979-7692		19791018
NL 190552	B	19931116			
NL 190552	C	19940418			
NO 7903349	A	19800422	NO 1979-3349		19791018
NO 152048	B	19850415			
NO 152048	C	19850724			
ES 485163	A1	19800616	ES 1979-485163		19791018
CA 1125749	A1	19820615	CA 1979-337955		19791018
PL 124063	B1	19821231	PL 1979-219034		19791018
SU 1402258	A3	19880607	SU 1979-2832177		19791018
PRIORITY APPLN. INFO.:			HU 1978-GO1426	A	19781019

IT 74950-18-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reactions of)
RN 74950-18-8 HCAPLUS
CN 5H-2,3-Benzodiazepin-7-ol, 1-(3,4-dimethoxyphenyl)-5-ethyl-8-methoxy-4-methyl- (9CI) (CA INDEX NAME)



IT 74950-20-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 74950-20-2 HCAPLUS
CN 5H-2,3-Benzodiazepin-7-ol, 1-(3,4-dimethoxyphenyl)-5-ethyl-8-methoxy-4-methyl-, monohydrochloride (9CI) (CA INDEX NAME)



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L8 ANSWER 19 OF 19 HCAPLUS COPYRIGHT 2007 ACS on STN
ED Entered STN: 12 May 1984
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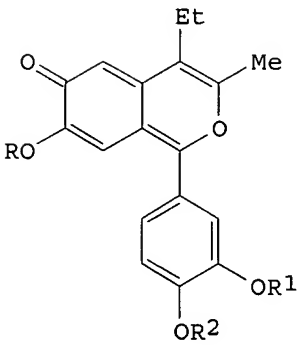

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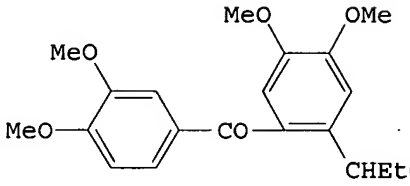

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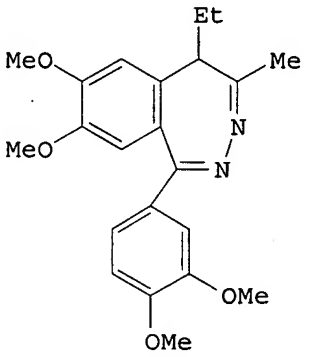


IV

AB The title compds. I (R, R1, R2 = H, Me) were prepared as intermediates for synthesis of benzodiazepines. Thus, the benzophenone II was cyclized to give 1-(3,4-dimethoxyphenyl)-3-methyl-4-ethyl-6-hydroxy-7-methoxybenzopyrrylium bromide (III), which was treated with Na2CO3 to give I (R = R1 = R2 = Me). I (R = R1 = R2 = Me) was cyclized with H2NH2.H2O to give the benzodiazepine IV. IV was also prepared from III and H2NNH2.H2O. The benzodiazepines had central nervous system activity. The narcotics

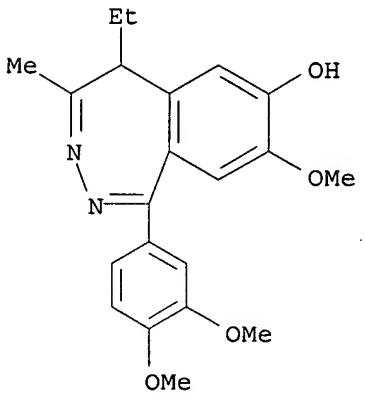
potentiator and spontaneous motor activity of the benzodiazepines was determined

ACCESSION NUMBER: 1980:550287 HCAPLUS <<LOGINID::20070319>>
DOCUMENT NUMBER: 93:150287
TITLE: 3',4',7-Substituted 1-aryl-3-methyl-4-ethyl-6H-2-benzopyran-6-one derivatives and their acid adducts
INVENTOR(S): Korosi, Jeno; Lang, Tibor; Szabo, Gabriella
PATENT ASSIGNEE(S): E. Gy. T. Gyogyszervegyeszeti Gyar, Hung.
SOURCE: Ger. Offen., 59 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 2940464	A1	19800424	DE 1979-2940464	19791005
HU 19079	A2	19801128	HU 1978-GO1422	19781005
GB 2031424	A	19800423	GB 1979-32418	19790919
GB 2031424	B	19821103		
FR 2438043	A1	19800430	FR 1979-24592	19791003
FR 2438043	B1	19830204		
CH 643253	A5	19840530	CH 1979-8900	19791003
FI 7903079	A	19800406	FI 1979-3079	19791004
JP 55066575	A	19800520	JP 1979-127437	19791004

PRIORITY APPLN. INFO.: HU 1978-GO1422 A 19781005
OTHER SOURCE(S): MARPAT 93:150287

IT 74950-20-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 74950-20-2 HCAPLUS
CN 5H-2,3-Benzodiazepin-7-ol, 1-(3,4-dimethoxyphenyl)-5-ethyl-8-methoxy-4-methyl-, monohydrochloride (9CI) (CA INDEX NAME)



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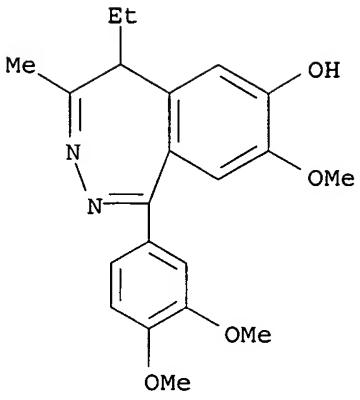
IT 74950-18-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation, alkylation, and narcotic potentiator activity of)
RN 74950-18-8 HCAPLUS
CN 5H-2,3-Benzodiazepin-7-ol, 1-(3,4-dimethoxyphenyl)-5-ethyl-8-methoxy-4-methyl- (9CI) (CA INDEX NAME)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OMe
OMe
OMe